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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Pharmaxis

By TIM BOREHAM

ASX code: PXS

Share price: 7.8 cents

Shares on issue: 549,139,613

Market cap: $42.8 million

Chief executive officer: Gary Phillips

Board: Malcolm McComas (chair), Mr Phillips, Dr Kathleen Metters, Dr Neil Graham

Financials (year to June 30, 2022): revenue from sale of goods $7.42 million (up 10%), milestones, sale of distribution rights $2.5 million, loss of $1.93 million (previous $3 million deficit), cash of $8.9 million (excludes $US5 million payment from Orbital device sale

Major shareholders: BVF Partners (Biotech Value Fund) 18.7%, Karst Peak Capital 12.4%, D & A Income 7.4%.

If there were a biotech award for making a silk purse out of a sow's ear, the accolade would go to Pharmaxis after September's funding deal to develop its anti-inflammatory compound for Parkinson's disease.

In this case, the porcine auditory organ was long-time Germanic partner Boehringer Ingelheim, which in 2019 handed back the rights to the liver disease NASH (fatty liver disease).

The compound worked fine with NASH, by targeting the relevant enzyme called semi-carbazide-sensitive amine oxidase (SSAO).

But Boehringer walked because it also inhibited a brain enzyme called monoamine oxidase B (MAOB).

Pharmaxis has turned the setback to its advantage by targeting MAOB as a Parkinson's treatment.

This month the approach was vindicated when Parkinson's UK extended a grant of up to $5 million for a clinical trial (see below).

"We are taking advantage of what Boehringer saw as a problem," says Pharmaxis chief Gary Phillips.

Last Monday, the company capped off an upbeat month by reporting encouraging results of a Perth-based trial to treat skins scarring for burns victims (also see below).

The company recently pocketed a handy $7 million by selling a delivery device that everyone had forgotten about - except for Mr Phillips (yep, see below as well).

In a GoldiLOX position

A biotech sector veteran, Pharmaxis is immersed in amine oxidase chemistry which is the backbone of several enzymes involved in inflammation and fibrosis.

The company's target is pan-lysyl oxidase (LOX), an enzyme closely implicated in inflammation and fibrosis.

The company's lead program tackles the rare blood cancer myelofibrosis.

Pharmaxis has also commercialized Bronchitol, a powder to relieve the lung congestion of cystic fibrosis sufferers.

It also sells a second-string product called Aridol, for asthma diagnosis (both are made from the sugar mannitol).

The company's early impetus revolved around Bronchitol, but sales have been useful rather than company-making. Since then, the company has focused on its multi-pronged clinical efforts.

Pharmaxis listed on the ASX in 2006, raising $25 million at 50 cents a share. A secondary listing on the Nasdaq was abandoned in 2009 for cost reasons.

The company's compounds come in three iterations: PXS-4728 (for Parkinson's disease), PXS-6302 (scarring) and PXS-5505 (myelofibrosis and hepatocellular carcinomas).

Parkinson's unwanted guest

Pharmaxis doesn't intend to treat Parkinson's directly with PXS-4728, but to target a precursor condition called idiopathic rapid eye movement sleep disorder (IRBD).

IRBD sufferers thrash about and cry out in their sleep as they live out their dreams (or nightmares).

The disorder can precede motor cognition dysfunction by up to 20 years, with 70 percent of sufferers going on to develop neurogenerative diseases such as Parkinson's disease.

Monoamine oxidase B (MAOB) is elevated in Parkinson's sufferers, resulting in lower dopamine levels that are a hallmark of the disease (current MAOB inhibitors on the market seek to increase dopamine production).

The problem with Parkinson's disease is that by the time it is diagnosed, about 80 percent of the dopaminergic neurons are gone.

"The horse has already left the stable," Mr Philips says. "At that point all we can try to do is to rescue the remaining cells and boost the amount of dopamine available to these patients."

Mr Phillips says while carrying out two phase II studies - and 11 studies in all - Boehringer identified the "off target effect" of inhibiting MAOB.

While the MAOB targeting effect wasn't deemed a safety issue, Boehringer decided it made developing a liver (NASH) drug more complex and expensive.

"It would have increased the cost of marketing a NASH drug as the MAOB effect would have needed to be monitored," Mr Phillips says.

The deal

Under the auspices of Parkinson's Virtual Biotech, Parkinson's UK is extending up to GBP2.9 million ($A4.8 million) to Pharmaxis, for a phase II trial.

The double-blinded, placebo-controlled effort aims to enrol 40 idiopathic rapid eye movement sleep disorder (IRBD) patients, at sites at the University of Sydney and University of Oxford.

"If we could stop IRBD we would reduce number of Parkinson's patients in UK by one third," Mr Phillips says.

In return for the moolah, Parkinson's UK is entitled to royalties capped at four times its investment for neurological indications; and two times for other diseases.

Pharmaxis will supply the drug and, handily, Boehringer has 200 kilograms of the stuff - now surplus to requirements - in a German warehouse.

Myelofibrosis update

Suffered by one in 500,000 citizens, myelofibrosis is a scarring of the bone marrow that interrupts the normal production of white and red blood cells and platelets.

Myelofibrosis sufferers typically are aged 50 to 80 years and can expect to live an average of only five years. About 10 percent will go on to develop leukemia.

Granted an orphan drug designation by the US Food and Drug Administration in 2020, PXS-5505 targets the matrix [inflammation] formation in the bone marrow and thus modifies the disease.

Currently, myelofibrosis is treated by a class of drugs called JAK (Janus kinase) inhibitors that provide symptomatic relief but do not ameliorate the disease. They also cause unpleasant side effects.

Pre-clinical models showed that PXS-5505 reversed the bone marrow fibrosis.

Carried out at sites in Australia, South Korea, Taiwan and the US, a 24-patient, phase II study began dosing in March last year.

The main endpoint is to show the drug is safe and well tolerated as a monotherapy for patients intolerant of, or unresponsive to, current JAK inhibitors.

Interim results are expected before the end of the year, with full results slated for the first half of 2023.

Burns trial runs hot

The company is also targeting burns-related scarring, in league with Perth burns legend Prof Fiona Wood and other esteemed researchers at the Fiona Stanley Hospital. (Prof Wood shot to fame for her work with spray-on skin – now Avita's Recell - for the survivors of the Bali Bombings exactly two decades ago.)

It's hoped that Pharmaxis' compound PXS-6302, which it discovered in its own labs, will suppress the enzymes responsible for such scarring.

This week, the company said that interim results from the first eight of 50 planned patients showed "a high level of inhibition of enzymes and changes in biomarkers that are implicated in scarring".

On a bum note, four patients withdrew from the study after experiencing redness and itching. These adverse reactions appear to have been solved by reducing daily topical applications to three times per week.

The next stage involves 42 patients split into active and control cohorts, with final results from the investigator-led (that is, Prof Woods) study expected in mid-2023.

Bronchitol rolls on

An inhaled dry mannitol powder, Bronchitol has been approved in US, Europe, Australia, Brazil, South Korea and Russia as a treatment for cystic fibrosis.

The most common inherited disease, cystic fibrosis results in the build-up of dry mucus in the lungs, which inhibits breathing and causes infection. While life expectancy is improving, sufferers can only expect to live to their forties.

A key advantage of Bronchitol is that it is portable and doesn't require a nebulizer.

The FDA approval process was not easy, with the agency ordering the company to do a second phase III trial in 2013. Sagely, Pharmaxis partnered with the Italian based Chiesi which holds the US rights and bears all clinical and most regulatory costs.

Pharmaxis is entitled to double digit royalties and a manufacturing margin. Bravo!

Finances and performance

Sometimes the dormant assets in the bottom drawer are well worth remembering.

A few years back, Pharmaxis bought a dry powder inhaler called Orbital from a Briton who invented the device in a shed at his house in Nottingham. (Mr Phillips recalls the deal was sealed over cucumber sandwiches made by the chap's wife).

Capable of delivering 400 milligrams of powder without reloading, Orbital was intended to increase Bronchitol's commercial life, but Pharmaxis' attention turned elsewhere.

Mr Phillips dusted off the asset and hawked it to US drug delivery house Aptar Group, for $US5 million ($A7 million) cash. Pharmaxis can still use the device for administering Bronchitol, royalty free.

Pharmaxis reported cash of just under $9 million as of June 30, 2022, but with the Orbital proceeds and a $5 million Federal Research and Development Tax Incentive, the balance is now more like $21 million. The Parkinson's cash trickles in over the next 18 months.

Over the last 12 months, Pharmaxis shares have gyrated between14 cents (October last year) and 6.5 cents (June-July this year).

Not Russian away

Bronchitol is the only approved, reimbursed cystic fibrosis drug in Russia, with the pariah state accounting for almost half of the company's $5.81 million of Bronchitol revenue last year. The sales are via a Turkish distributor.

Mr Phillips says the board talked through the moral dilemma of selling to Russia, but decided that withdrawing would have been “petty and damaging” for patients.

“The right thing to do was not to block supply, but not to invest in the country,” he says. “If you are a Russian pulmonologist and want the best drug for your patient, Bronchitol is the only one effectively trialed and shown to be effective.”

Dr Boreham’s diagnosis:

Mr Phillips says the company is an “oddity” relative to its peers, in that it has a “really solid, internally-generated pipeline” and a revenue-generating respiratory franchise.

But investors have adopted the Shania Twain ‘don’t impress me much’ stance, with the stock valued at a derisory $20 million (market capitalization less cash).

“Our enterprise value actually dropped when we put the $7 million in the bank [from the Aptar deal],” laughs Mr Phillips, in that if-you-don’t-laugh-you-cry kind of way.

We suspect investors are punishing the company for sins of the past, including underwhelming Bronchitol sales, the shelving of internal programs and Boehringer bidding ‘auf wiedersehen’ (but not before handing $83 million in milestone payments to Pharmaxis).

The three recent strands of news flow suggest the company’s fortunes could be turning.

“I don’t know what I have to do to shift the share price, but I suspect delivering results from the next two clinical studies will be an explosive trigger,” Mr Phillips says.

In a world on a geopolitical knife edge, let’s hope it’s the only explosive trigger humanity will see.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. Sometimes his columns make a silk purse out of a sow’s ear; other times they are simply a pig’s ear.